

AMENDMENTS TO THE CLAIMS

1. (Original) An apparatus for noninvasive measurement of glucose through near-infrared spectroscopy, comprising:
- a base module comprising a grating and a detector array;
 - 5 a sampling module, securely and removeably attached to a sample site, and coupled to said base module, said sampling module comprising an illumination source;
 - an optic system located before and/or after said sample site for coupling said illumination source to said sample and said sample to said detector array;
 - 10 and
 - a communication bundle for carrying optical and/or electrical signals between said base module and said sampling module, and for carrying power to said sampling module from said base module.
- 15 2. (Original) The apparatus of Claim 1, said optic system comprising any of: an optical filter, a light blocker, and a standardization material.
3. (Original) The apparatus of Claim 1, said sampling module further comprising at least one of:
- 20 a low profile sampling interface;
 - a low wattage stabilized source in close proximity to said sampled site;
 - an excitation collection cavity or optics;
 - a guide;
 - a preheated interfacing solution;
 - 25 means for maintaining a temperature controlled skin sample;
 - a mechanism for constant pressure and/or displacement of sampled skin tissue;
 - a photonic stimulation source; and
 - collection optics or fiber.

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4. (Original) The apparatus of Claim 1, said sampling module further comprising:

5 a guide that is securely and removeably attached to said sampling site, said guide continuously and/or periodically physically and optically locating said sampling module relative to said sample site in a repeatable manner and with minimal disturbance to said sampling site.

5. (Original) The apparatus of Claim 4, further comprising:

10 means for pretreatment of said sample site to provide appropriate contact of said sampling module to said sampling site to reduce specular reflectance, to approach and maintain appropriate sampling site temperature variation, and to minimize sampling site hydration changes.

6. (Original) The apparatus of Claim 1, wherein said sampling module
15 collects a diffusely reflected or transflected signal from said sampling site.

7. (Original) The apparatus of Claim 1, either of said base module and said sampling module comprising any of:

20 a wavelength reference standard; and
an intensity reference standard.

8. (Original) The apparatus of Claim 1, wherein said communication bundle is integrated between said sampling module and said base module.

25 9. (Original) The apparatus of Claim 1, wherein said sampling module and said base module are integrated together into a handheld unit.

10. (Original) The apparatus of Claim 1, said sampling module comprising any of:

30 a housing, preferably made of silicon;
a reflector;

a lamp, preferably comprising a tungsten halogen source, coupled to said reflector; and

a photodiode for monitoring said lamp and for maintaining said lamp's output stable by means of a lamp output controller.

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11. (Original) The apparatus of Claim 10, wherein said reflector, and hence incident light emanating therefrom, is centered on an angle off of a normal to said sample site to allow room for a collection fiber.

10 12. (Original) The apparatus of Claim 10, wherein light is focused through a silicon window onto an aperture at said sample site, wherein said silicon window comprises a longpass filter.

13. (Original) The apparatus of Claim 4, wherein said sampling module
15 reversibly couples into said guide for reproducible contact pressure and/or sampling location.

14. (Original) The apparatus of Claim 13, said guide further comprising:
at least one magnet for aiding in positioning a sampling module probe to
20 ensure proper penetration of said probe into a guide aperture, and to enable a constant pressure and/or displacement interface of said sampling site;

wherein said magnet is optionally electrically activated to facilitate controlled movement into a guide aperture and to allow, through reversal of said magnet poles, withdrawal from said guide aperture without pulling.

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15. (Original) The apparatus of Claim 13, wherein said reversible coupling of said sampling module into said guide allows said sampling module to be removed and coupled to an intensity reference and/or a wavelength reference that have a same guide interface.

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16. (Original) The apparatus of Claim 15, wherein said intensity reference comprises a 99% reflective material, and wherein said wavelength reference is polystyrene.

5 17. (Original) The apparatus of Claim 1, said sampling module further comprising:

a heater for maintaining said sampling site at a constant temperature.

10 18. (Original) The apparatus of Claim 1, said sampling module further comprising:

a detection fiber for collecting diffusely reflected light.

15 19. (Original) The apparatus of Claim 1, wherein said base module either resides on a support surface, or said base module may be worn by a person.

20 20. (Original) The apparatus of Claim 1, wherein said sampling module couple to any of a hand, finger, palmar region, base of thumb, forearm, volar aspect of the forearm, dorsal aspect of the forearm, upper arm, head, earlobe, eye, tongue, chest, torso, abdominal region, thigh, calf, foot, plantar region, and toe.

21. (Original) The apparatus of Claim 1, further comprising:
a docking station for said base module.

22. (Original) The apparatus of Claim 1, wherein said base module is coupled
25 directly to said sampling module, with said communication bundle forming an integral part thereof.

23. (Original) The apparatus of Claim 1, wherein said sampling module further comprises:
30 a housing, preferably providing a minimum of 6 O.D. blocking in ultraviolet, visible, and near-IR from 700 to 1000 nm.

24. (Original) The apparatus of Claim 23, wherein said housing is constructed of silicon, and preferably has a thickness of about 1mm.
- 5 25. (Original) The apparatus of Claim 1, said illumination source comprising:
a tungsten halogen source ranging in power from 0.05 W to 5 W.
26. (Original) The apparatus of Claim 1, said illumination source comprising:
at least one light emitting diode (LED).
- 10 27. (Original) The apparatus of Claim 1, further comprising:
a photodiode; and
a feedback controller for allowing said illumination source to be driven at
different levels at different points in time during and prior to data acquisition;
15 wherein said photodiode is placed before an optional order sorter to detect
visible light from said illumination source; and
wherein said photodiode comprises any of a silicon, InGaAs, InPGaAs,
PbS, and PbSe detector.
- 20 28. (Original) The apparatus of Claim 1, said illumination source further
comprising:
a reflector having any of a parabolic, elliptical, and spherical shape.
29. (Original) The apparatus of Claim 29, wherein said source, said housing,
25 and said reflector are arranged to bring in source light nearly parallel to said
sample site surface.
30. (Original) The apparatus of Claim 1, wherein said sampling module further
comprising:

folding optics for bringing light in at a low angle relative to said sampling site surface, wherein said folding optics optionally comprise any of a mirror and a focusing mirror.

- 5 31. (Original) The apparatus of Claim 1, said communication bundle further comprising:

quick connect optics which comprise:

a first collection optic that is fixed into said communication bundle;

and

- 10 a connector in said communication bundle for accepting a second collection optic that in turn couples to said base module.

32. (Original) The apparatus of Claim 31, further comprising:

- 15 at least one optical device for coupling light by any of magnifying and demagnifying lenses and folding mirrors.

33. (Original) The apparatus of Claim 32, wherein said second collection optic is readily removed from said sampling module, allowing said sampling module to remain in contact with said sampling site.

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34. (Original) The apparatus of Claim 1, wherein said illumination source further comprises a heat source.

35. (Original) The apparatus of Claim 1, further comprising:

- 25 an optical filter located between said illumination source and said sampling site.

36. (Original) The apparatus of Claim 35, wherein said optical filter is located after said illumination source but not in contact with any of said sampling site and

30 a coupling fluid.

37. (Original) The apparatus of Claim 35, wherein said optical filter comprises:
at least two filters located between said illumination source and said
sampling site, wherein a first filter removes heat, and wherein a second filter
reduces spectral reflectance.

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38. (Original) The apparatus of Claim 35, wherein said optical filter comprises:
a silicon filter for removing light under 1050 nm, wherein a grating can be
used in the 1150 to 1850 nm region without detection of second or higher order
light off of said grating, wherein said silicon filter is placed before the grating and
after said sampling site.

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39. (Original) The apparatus of Claim 35, wherein said optical filter comprises:
a filter comprising of any of the following:

a filter that is a silicon longpass optic;

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a filter that is coated to block particular regions, in particular 1900 to 2500
nm;

a filter that is antireflection-coated to match refractive indices and
increase light

throughput, and/or used in combination with other filters, in particular shortpass
filters;

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a filter that is coated with a blocker for removing a largest intensity of a
black body curve of a typical tungsten halogen source that is not blocked by
silicon, wherein said blocking band may cover any region from about 1800 nm on
up to 3000 nm; and

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a filter that is used in combination with an RG glass that cuts off at about
2500 nm to provide a bandpass filter passing light from approximately 1100 to
2500 nm, wherein said filter combination is optionally used in conjunction with a
coating layer, in particular a blocker from 1900 to 2500 nm, to provide a
bandpass from 1100 to 1900 nm.

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40. (Original) The apparatus of Claim 1, said sampling module further comprising:

5 a member shaped into a parabolic optic surrounding part of said illumination source, wherein an outside of said member is coated with a reflector, in particular gold.

41. (Original) The apparatus of Claim 40, wherein said member is made of any of silicon and plastic.

10 42. (Original) The apparatus of Claim 1, said sampling module further comprising:

an illumination source filament that is wrapped around a collection fiber; and

15 a reflector for directing light into an aperture for admission therethrough to said sampling site, wherein said reflector optionally is any of surface coated for reflectance on an incident light surface, and transmissive with an outer surface of said reflector being reflectively coated.

43. (Original) The apparatus of Claim 42, further comprising:

20 a window defined between said illumination source and said sampling site, said window optionally comprising a filter.

44. (Original) The apparatus of Claim 1, said sampling module further comprising:

25 a broadband source operatively combined with a single element detector.

45. (Original) The apparatus of Claim 1, said sampling module further comprising:

30 a Fabry-Perot interferometer, and in particular a Fabry-Perot etalon.

46. (Original) The apparatus of Claim 1, said sampling module comprising:

a surface defining an aperture for providing optical pathlengths within a sample for indirectly monitoring glucose concentrations within a body, providing acceptable energy delivery to said sampling site, and providing appropriate heating/temperature control of said sampling site;

5 wherein variation of said aperture affects a net analyte signal of a sampled tissue.

47. (Original) The apparatus of Claim 46, further comprising:

10 a fiber optic collection fiber placed in a center of an illumination area defined by said aperture.

48. (Original) The apparatus of Claim 46, further comprising:

15 means for performing an indirect determination of glucose from sample constituents which comprise any of fat, protein, and water and that are distributed as a function of depth in a sample, wherein a magnitude of an indirect signal varies with said aperture.

49. (Original) The apparatus of Claim 1, wherein said sampling module is semi-permanently attached to said sampling site with a replaceable adhesive.

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50. (Original) The apparatus of Claim 46, further comprising:

a removable plug for placement in said aperture to stabilize tissue at said sampling site by providing a same tissue displacement as a probe.

25 51. (Original) The apparatus of Claim 46, further comprising:

a contact window for allowing a continuous barrier for hydration of said sampling site and a constant pressure interface.

52. (Original) The apparatus of Claim 1, sampling module further comprising

30 any of:

means for any of photonic stimulation, ultrasound pretreatment, mechanical stimulation, cooling, and heating.

53. (Original) The apparatus of Claim 1, sampling module further comprising
5 any of:

an LED for providing photonic stimulation to induce capillary blood vessel dilation.

54. (Original) The apparatus of Claim 1, further comprising:

10 a coupling fluid, preferably fluorinert, disposed between said sampling module and said sampling site for coupling incident photons into a tissue sample, wherein said coupling fluid is optionally preheated to minimize changes to a surface temperature of said sampling site, and minimize spectral changes observed from said tissue sample, wherein said coupling fluid, if preheated, is
15 preheated using any of illumination source energy, sampling site heater energy, and an auxiliary heat source.

55. (Original) The apparatus of Claim 55, further comprising:

means for automated delivery of said coupling fluid prior to sampling.

56. (Original) The apparatus of Claim 1, said sampling module further comprising:

a collection fiber placed into an aperture formed through a base, said collection fiber being in contact with a sampling site surface.

57. (Original) The apparatus of Claim 1, further comprising:

means for using any of a signal and an absence of observed intensity at large water absorbance bands near 1450, 1900, and 2500 nm to determine when said sampling module is in good spectral contact with a sampling site surface.

58. (Original) The apparatus of Claim 1, wherein said base module further comprises:

5 a two-way wireless communication system for transferring data between said base module and any of said sampling module and a data collection/processing system.

59. (Original) The apparatus of Claim 1, further comprising:

10 means for standardizing a wavelength axis of near-IR based on a comparative analysis of a master and slave spectra of a standardization material.

60. (Original) The apparatus of Claim 59, said means for standardizing comprising:

15 a material having absorption bands in a targeted wavelength region for determining said x-axis, said material comprising any of polystyrene, erbium oxide, dysprosium oxide, and holmium oxide.

61. (Original) The apparatus of Claim 59, wherein said material used for standardization is any of:

20 measured external to said base module;
measured continuously and mounted within said base module in a separate light path, wherein said internal wavelength standard is measured simultaneously with said sample;

25 moved through an actuator into a main optical train at an appropriate time;
wherein a reference spectrum is collected in any of a transmittance mode, reflectance mode, or a diffuse reflectance mode.

62. (Original) The apparatus of Claim 59, further comprising:

30 means for measuring a reference spectrum and a (wavelength) standardization spectrum through spectroscopic measurement of a non-absorbing material and a material with known and immutable spectral absorbance bands, respectively.

63. (Original) The apparatus of Claim 62, said means for measuring further comprising:

a master spectrum of a standardization material; and

means for determining a discrepancy between said master spectrum and an instrument standardization spectrum;

wherein said master spectrum and wavelength regions are optionally stored in a nonvolatile memory.

64. (Original) The apparatus of Claim 63, wherein at least one window across a spectrum of said x-axis phase shift between said master spectrum and an acquired spectrum are determined through a cross-correlation function after removing instrument related baseline variations, wherein said phase shift is used to correct (standardize) said x-axis of said acquired spectrum to said master spectrum.

65. (Original) The apparatus of Claim 1, said base module further comprising:
means for bias correcting spectral data collected in one or both of the X (spectra) and Y (glucose concentration) data.

66. (Original) The apparatus of Claim 1, said base module further comprising:
means for calibrating to an individual or a group of individuals based upon a calibration data set comprised of paired data points of processed spectral measurements and reference biological parameter values.

67. (Original) The apparatus of Claim 66, wherein for glucose measurement, said reference values comprise at least one of the following: finger capillary blood glucose, alternate site capillary blood glucose at a site on the body other than the finger, interstitial glucose, or venous blood glucose.

68. (Original) The apparatus of Claim 1, wherein said base module is integrally connected to a docking station; wherein said docking station comprises a computer and a glucose management center; wherein said glucose management center keeps track of events occurring in time which may include
5 any of glucose intake, insulin delivery, and determined glucose concentration.

69. (Original) The apparatus of Claim 1, said base module further comprising:
means for estimating precision of measurement through a statistical analysis of repeated or successive measurements; and
10 means for determining when a biological parameter is close to a preset level through a statistical estimate of confidence limits of a future analyte prediction made through a simple slope (change in said biological parameter over change in time) estimate based on an exponentially moving average, where said confidence limits are based upon said estimate of precision.

15 70. (Original) The apparatus of Claim 1, said base module further comprising:
means for determining when a biological parameter is close to a preset level through a standard time series analysis; wherein an alarm is invoked if an associated present alarm level is within a confidence interval of a future
20 biological parameter prediction.

71. (Original) The apparatus of Claim 1, either of said sampling module and said base module further comprising:
means for taking any of continuous and semi-continuous measurements
25 when said sampling module is in contact with said sampling site.

72. (Original) The apparatus of Claim 1, said base module further comprising:
means for using time based information and trends to perform various functions, which may include any of estimate of precision, confidence intervals,
30 and prediction of future events.

73. (Original) The apparatus of Claim 1, further comprising:

a link provided to an insulin delivery system to provide a feedback mechanism for control purposes.

5 74. (Original) The apparatus of Claim 1, any of said base module and said sampling module comprising:

a spectrometer system comprising LED's to provide near-infrared radiation to said sample site over predefined wavelength ranges, wherein each of said LED's provides near-infrared radiation over a band of wavelengths.

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75. (Original) The apparatus of Claim 74, wherein wavelengths of said LED's are selected specifically to optimize a signal-to-noise ratio of a net analyte signal of a target analyte, and are arranged at various distances with respect to detection elements to provide a means for sampling various tissue volumes for purposes of averaging and determination of a differential measurement.

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76. (Original) The apparatus of Claim 74, wherein said LED's are sequentially energized one at a time and/or in groups to obtain various estimates of diffuse reflectance of various tissue volumes at specific wavelengths or bands of wavelengths.

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77. (Original) The apparatus of Claim 74, wherein said LED's are pulsed to provide short measurements with high signal-to-noise ratios to provide greater illumination intensity while avoiding photo heating of a sampled tissue volume.

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78. (Original) The apparatus of Claim 74, wherein said LED's are modulated at a particular duty cycle and frequency to remove additive noise and to provide simultaneous measurement of multiple wavelengths.

30 79. (Original) The apparatus of Claim 74, wherein said LED's illuminate said sample site directly.

80. (Original) The apparatus of Claim 74, further comprising:

a mixing chamber with a reflective surface located between said LED's and an optical window to provide a nearly uniform distribution onto a sample
5 tissue region surrounding a detection fiber, wherein each LED is optionally recessed into a material having a reflective surface.

81. (Original) The apparatus of Claim 74, wherein groups of LED's are employed with each group associated with a single filter type, and wherein said
10 LED's are arranged at distances surrounding a detection fiber and energized to enable detection of light associated with different wavelength bands and different illumination to detection distances.

82. (Original) The apparatus of Claim 81, wherein said groups of LED's are
15 arranged in any of:

annuli (rings) at specific distances surrounding said detection fiber, wherein said filters are arranged in rings surrounding said detection fiber and covering associated LED's; and

wedges surrounding said detection fiber, wherein said filters are either of a
20 wedged or triangular shape and are arranged to cover associated LED's.

83. (Original) The apparatus of Claim 81, wherein each LED or group of LED's has an associated optical filter that is used to limit a bandwidth of emitted light, wherein a different filter is mounted such that light emitted and delivered to said
25 sampling site from said LED passes through said filter, wherein a filter associated with an LED has a specific bandwidth and is centered on a particular wavelength that is within a native bandwidth of said LED, wherein groups of LED's are optionally associated with a same filter.

30 84. (Original) The apparatus of Claim 81, wherein said LED's have a bandwidth relatively broader than net analyte and interference signals.

85. (Original) The apparatus of Claim 81, wherein said LED's are used in a spectrometer without a dispersive element and a single element detector, wherein thin dielectric films are used as in Fabry-Perot interference filters and a filter is associated with each LED.

86. (Original) The apparatus of Claim 1, said optic system comprising a plurality of optical probes, wherein an optical probe includes:
one or more optical paths for incident radiation;
one or more detection fibers for each of said optical paths; and
a spacer having a radial dimension that establishes a minimum distance between said incident radiation and said one or more detection fibers;
wherein a maximum penetration distance of said incident radiation is greater than said radial dimension.

87. (Original) The apparatus of Claim 86, wherein nearest neighbor optical probes are uniformly a minimum distance from each other, so that the collection of light from a targeted depth in a tissue sample is maximized and interference from other depths is minimized.

88. (Original) The apparatus of Claim 86, wherein said optic system includes at least two of said optical probes.

89. (Original) The apparatus of Claim 86, wherein said optics system includes either three or five of said optical probes.

90. (Original) The apparatus of Claim 86, wherein each optical probe is positioned to be at least 8 mm distant from its nearest neighbor.

91. The apparatus of Claim 86, wherein said radial dimension is from approximately 50 μm to approximately 3000 μm .

92. (Original) The apparatus of Claim 91, wherein said radial distance is approximately 100 μm .

5 93. (Original) The apparatus of Claim 91, wherein said radial distance is approximately 200 μm .

94. (Original) The apparatus of Claim 91, wherein said radial distance is approximately 300 μm .

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95. (Original) An optical probe, comprising:
one or more optical paths for incident radiation;
one or more detection fibers for each of said optical paths; and
a spacer having a radial dimension that establishes a minimum distance
15 between said incident radiation and said one or more detection fibers;
wherein a maximum penetration distance of said incident radiation is
greater than said radial dimension.

20 9796. (Currently amended) The apparatus of Claim 9695, wherein said radial distance is from approximately 50 μm to approximately 3000 μm .

9897. (Currently amended) The apparatus of Claim 9796, wherein said radial distance is approximately 100 μm .

25 9998. (Currently amended) The apparatus of Claim 9796, wherein said radial distance is approximately 200 μm .

40099. (Currently Amended) The apparatus of Claim 9796, wherein said radial distance is approximately 300 μm .

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